ABSTRACT OF THE DISCLOSURE

The present invention provides a cobalamin-drug conjugate suitable for the treatment of tumor related diseases. Cobalamin is indirectly covalently bound to an anti-tumor drug via a cleavable linker and one or more optional spacers. Cobalamin is covalently bound to a first spacer or the cleavable linker via the 5'-OH of the cobalamin ribose ring. The drug is bound to a second spacer of the cleavable linker via an existing or added functional group on the drug. After administration, the conjugate forms a complex with transcobalamin (any of its isoforms). The complex then binds to a receptor on a cell membrane and is taken up into the cell. Once in the cell, an intracellular enzyme cleaves the conjugate thereby releasing the drug. Depending upon the structure of the conjugate, a particular class or type of intracellular enzyme affects the cleavage. Due to the high demand for cobalamin in growing cells, tumor cells typically take up a higher percentage of the conjugate than do normal non-growing cells. The conjugate of the invention advantageously provides a reduced systemic toxicity and enhanced efficacy as compared to a corresponding free drug.